рл. No. 09/839,574; Group Art Unit: 1646 kt. No. 1530.0180002/EKS/EJH;

nventors: Manthorpe et al.; Tel: 202/371-2600 itle: Compositions and Methods for in vivo Delivery of olynucleotide-Based Therapeutics

PLASMID GENE PARENTAL PROMOTOR/ TERMINATOR NAME **PLASMID ENHANCER** VR1223 FIREFLY LUX VR1012* CMV **BGH** VR1412 BACTERIAL LACZ VR1012* **CMV BGH** VR2901 MOUSE EPO VR1012* CMV **BGH** VR2996 MOUSE EPO VR1012 MV/Desmin **BGH** VR3301 HUMAN SEAP VR1012* CMV **BGH** VR3502 RAT PROINSULIN VR1012* **CMV BGH** VR4151 HUMAN IFN-OMEGA VR1055 CMV mRBG VR4700 INFLUENZA NP VR1255** CMV mRBG **VR1418** BACTERIAL LACZ VR1043 **RSV BGH** VR1255 FIREFLY LUX VR1223 **CMV** mRBG INTERMEDIATE PLASMIDS VR1012 NONE V1J*** CMV

VR1343

VR1255

RSV

CMV

BGH

BGH

mRBG

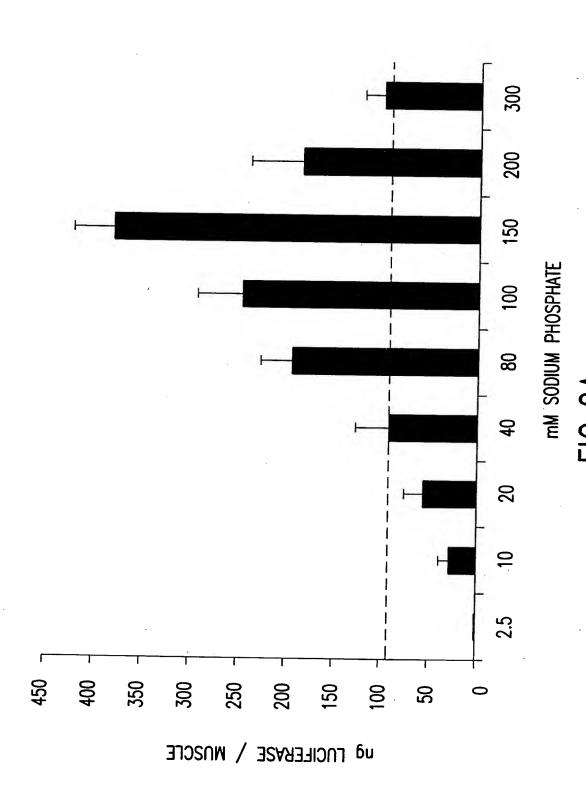
FIG. 1

NONE

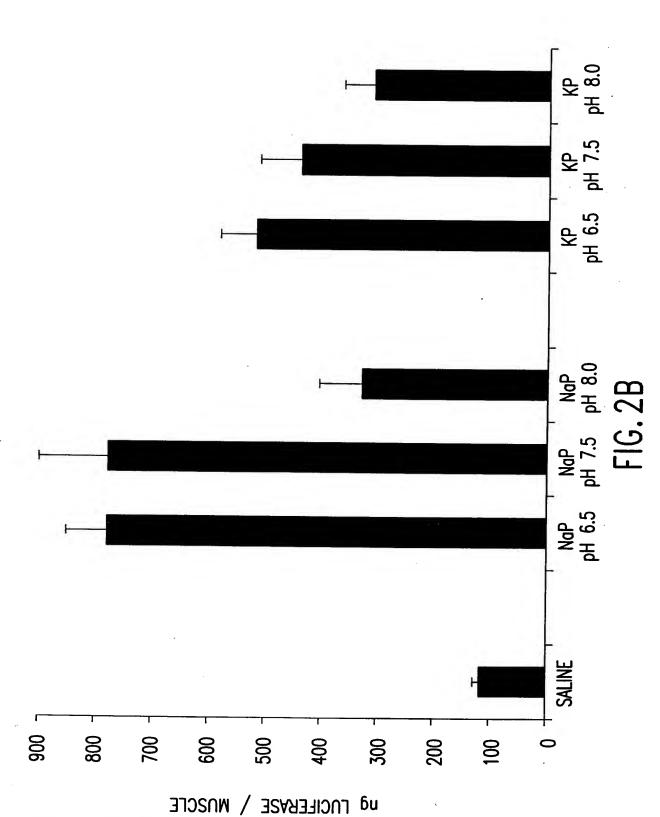
NONE

VR1043

VR1055



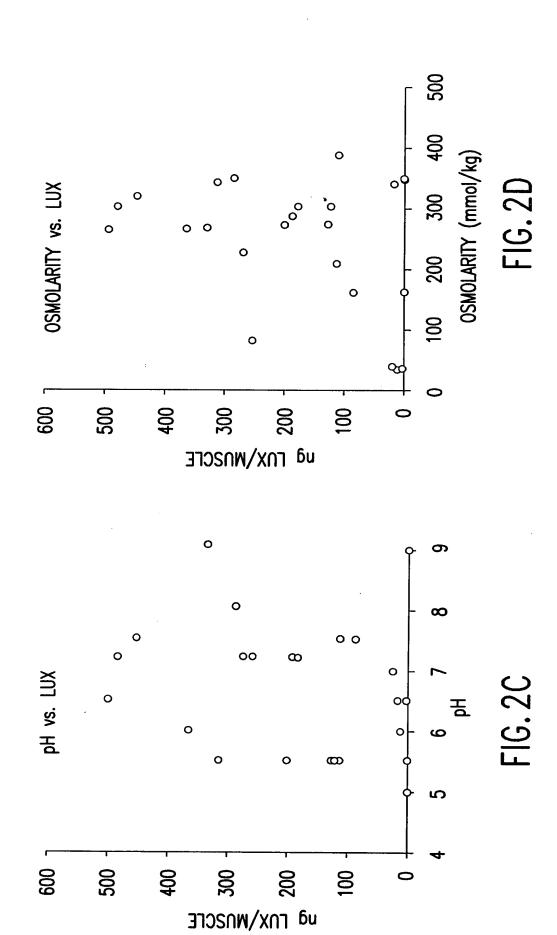
Appl. No. 09/839,574; Group Art Unit: 1646
Dkt. No. 1530.0180002/EKS/EJH;
Inventors: Manthorpe et al.; Tel: 202/371-2600
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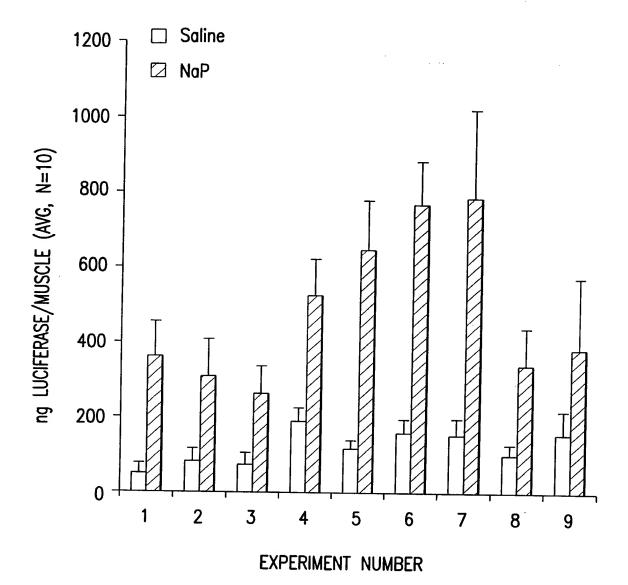
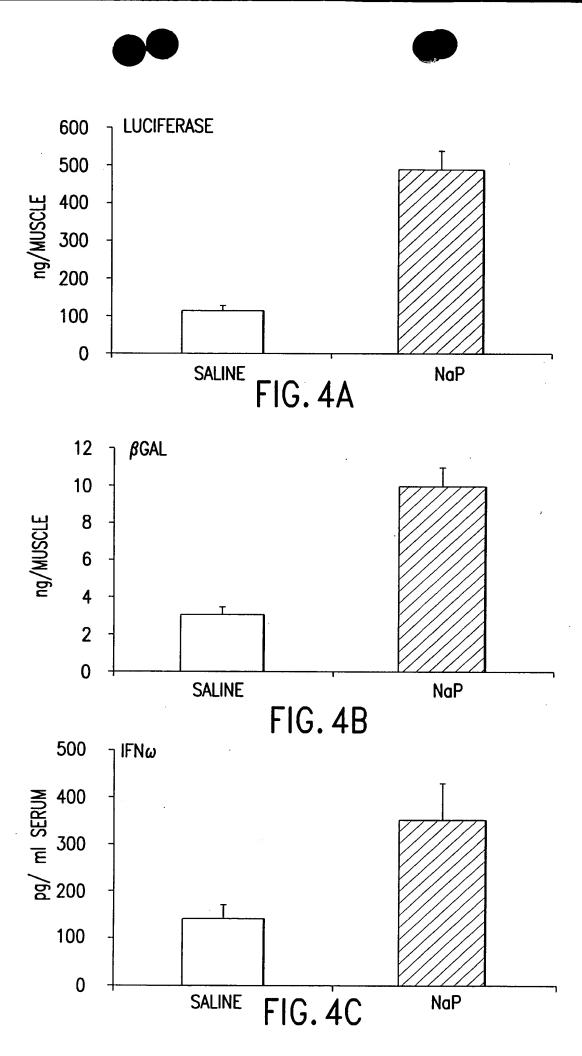
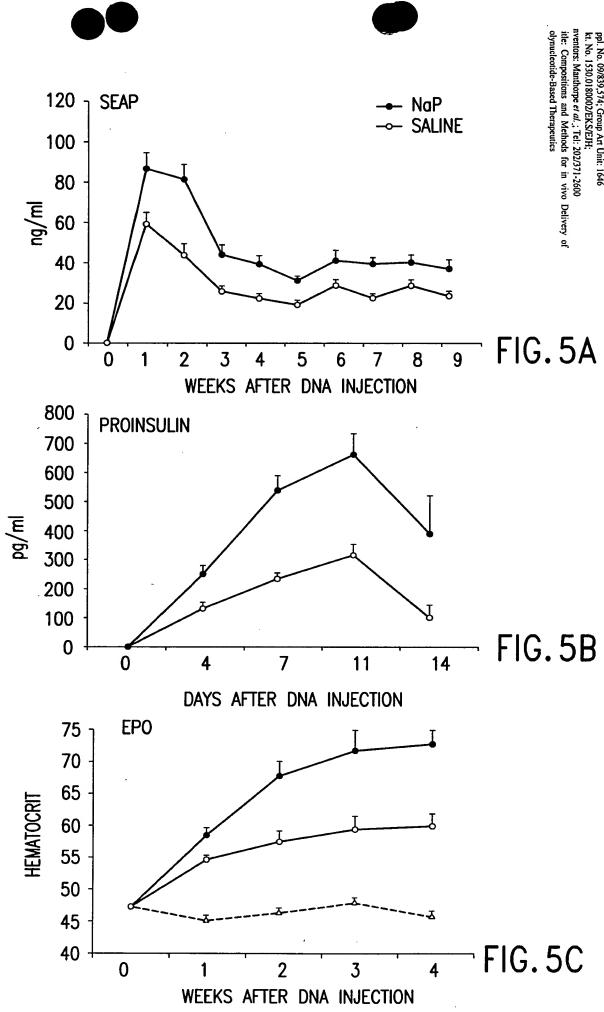


FIG.3



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Polynucleotide-Based Therapeutics



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FIG.6A



FIG.6B



FIG.6C



FIG.6D

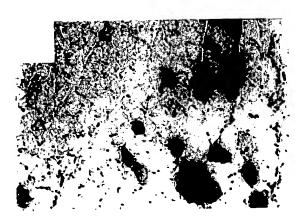


FIG.6E



FIG.6F

0

SALINE

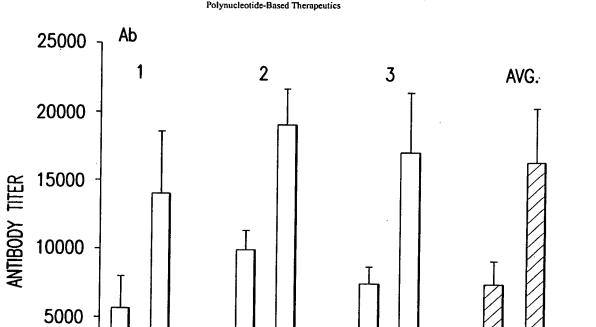
NaP

SALINE

NaP

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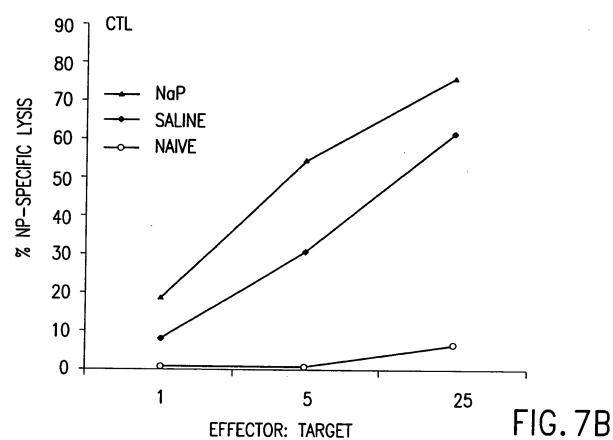
SALINE

NaP

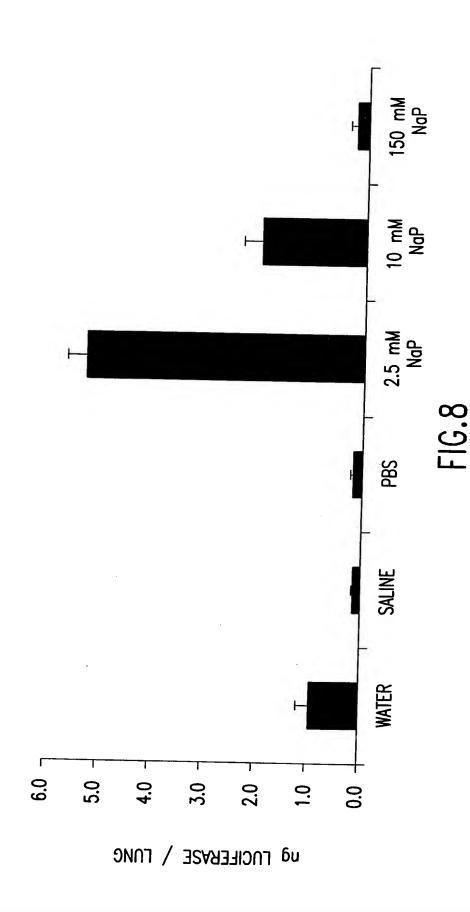
FIG. 7A

SALINE

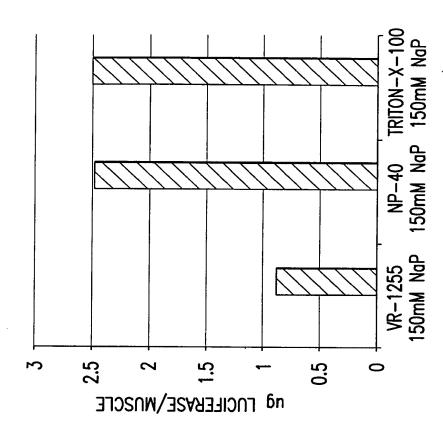
NaP



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Dki. No. 1530.0180002/EKS/EJH;
Inventors: Manthorpe et al.; Tel: 202/371-2600
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VR-1255 NP-40 TRITON-X-100 154mM NaCl 9: 1.2 1.4 0.8 9.0 0.2 0.4 0

nd FUCIFERASE/MUSCLE

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P104 3
TRITON X-10 3
NP-40 3
L81 3
P103 3
P105 3
F108 3
L121 3
P65 4
L31
F68 5
L64 5
25R4 5
L101 5
L44 5
L101 5
L62 6
25R2 7

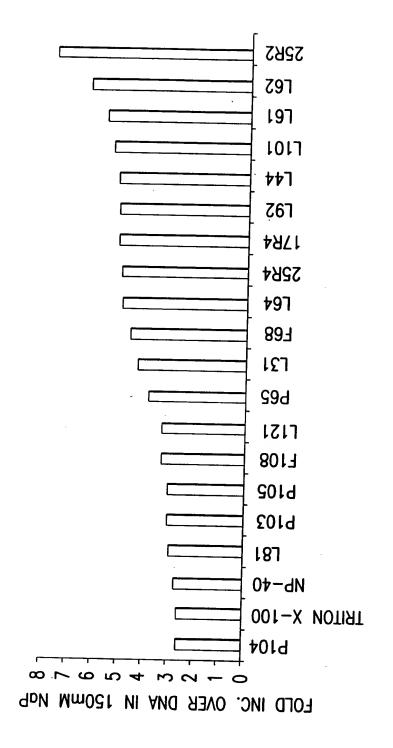
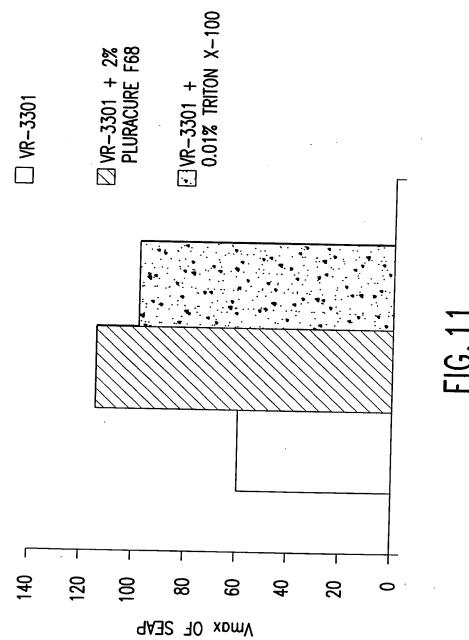


FIG. 10

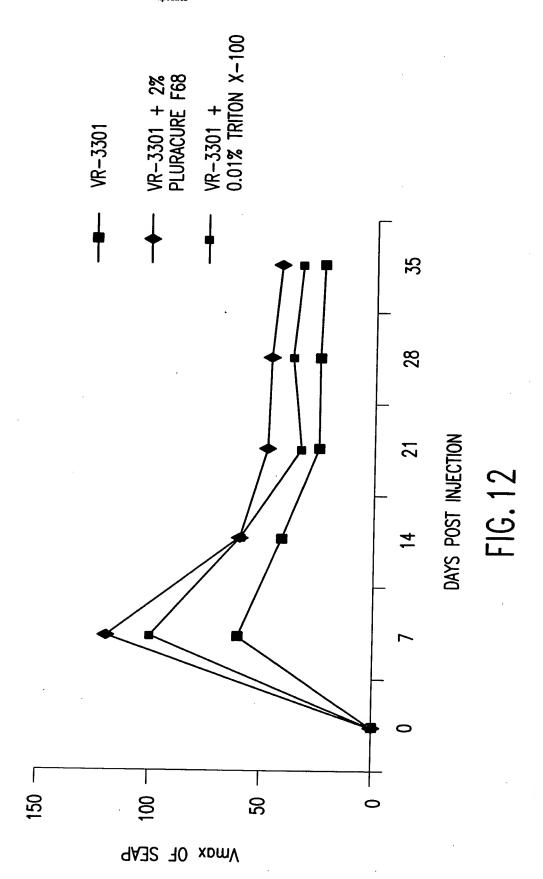


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appl. No. 09/839,574; Group Art Unit: 1646
Dkt. No. 1530.0180002/EKS/EJH;
Inventors: Manthorpe et al.; Tel: 202/371-2600
Title: Compositions and Methods for in vivo Delivery of Polynucleotide-Based Therapeutics



ngg-china and and

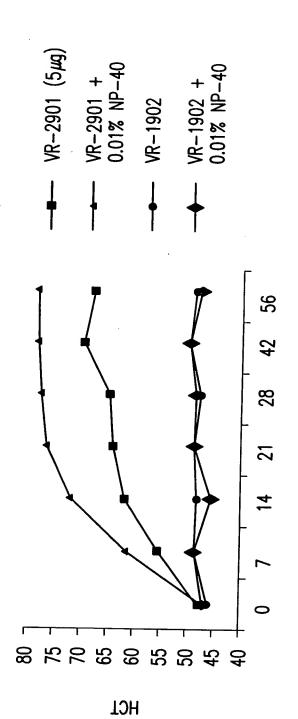


FIG. 13

DAYS POST INJECTION

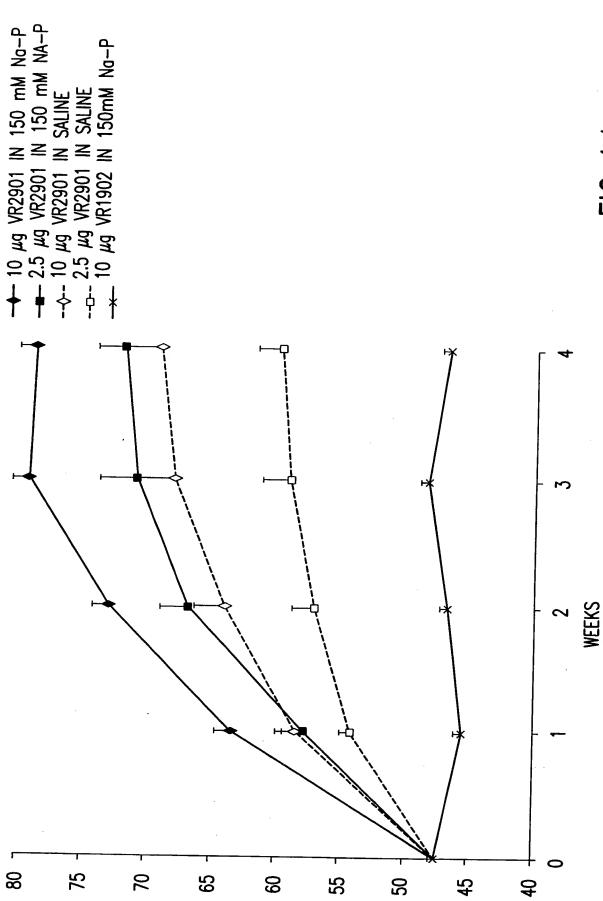
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Inventors: Manihorpe et ed. ; Tel: 202/371-2600
Polynucleotide-Based Therapeutics

Appl. No. 09/839,574; Group Ari Unit: 1646 Dkt. No. 1530.0180002/EKS/EJH;

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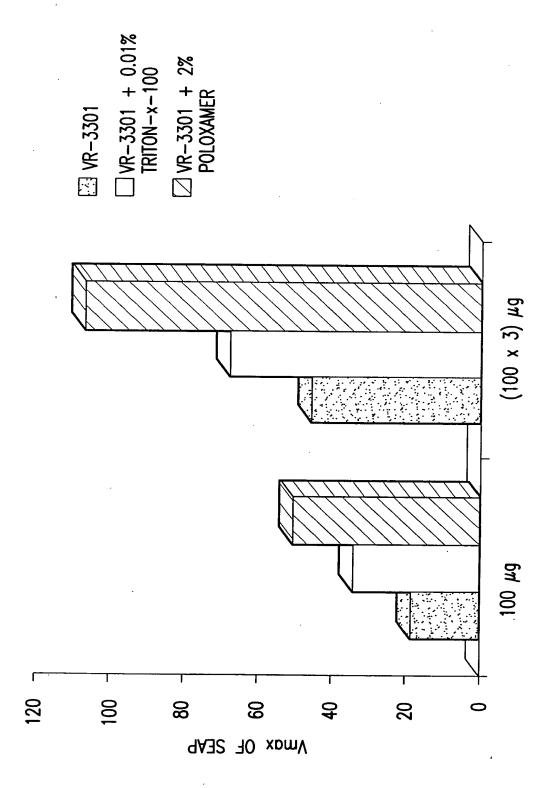
ppl. No. 09/839,574; Group Art Unit: 1646 kt. No. 1530.0180002/EKS/ELH; nventors: Manthorpe et al.; Tel: 202371-2600 itle: Compositions and Methods for in vivo Delivery of olynucleotide-Based Therapeutics



AVERAGE HEMATOCRIT

FIG. 14

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Inventors: Manthorpe et al.; Tel: 202/371-2600
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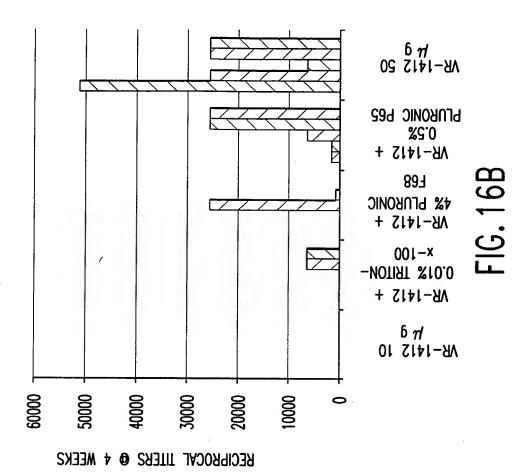
Appl. No. 09/839,574; Group Art Unit: 1646

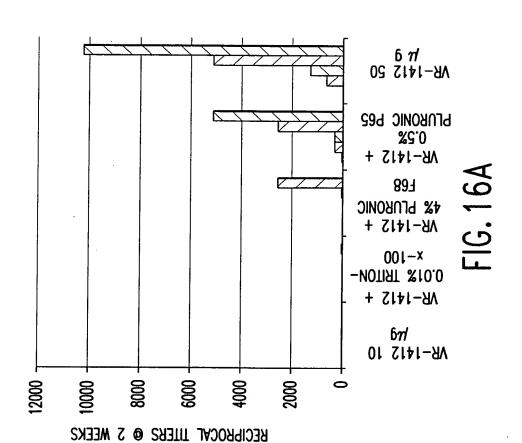
Dkt. No. 1530.0180002/EKS/EJH;

Inventors: Manthorpe et al.; Tel: 202/371-2600

Title: Compositions and Methods for in vivo Delivery o

Polynucleotide-Based Therapeutics

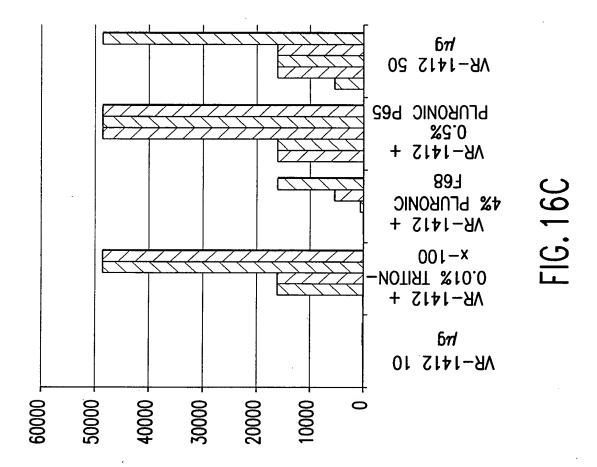




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ppl. No. 09/839,574; Group Ari Unit: 1646 Kt. No. 1530.0180002/EKS/EJH; nventors: Manthorpe et al.; Tel: 202/371-2600 itle: Compositions and Methods for in vivo Delivery of olynucleotide-Based Therapeutics

RECIPROCAL TITERS @ 10 WEEKS



CTL ACTIVITY IS NOT INHIBITED WHEN pDNA + POLOXAMER IS ADMINISTERED

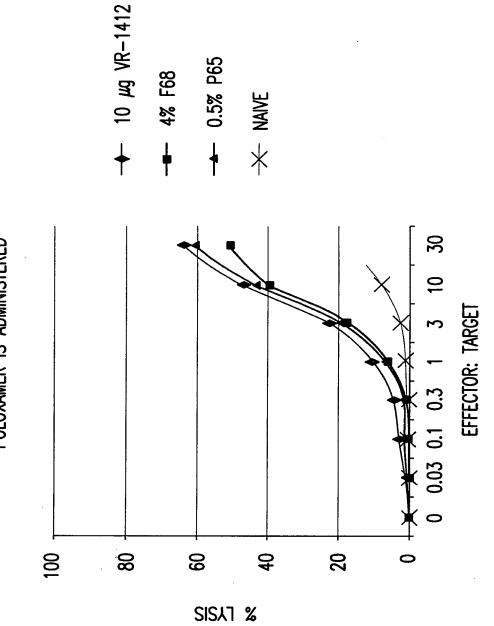


FIG. 16D

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Inventors: Manthorpe et al.; Tel: 202/371-2600

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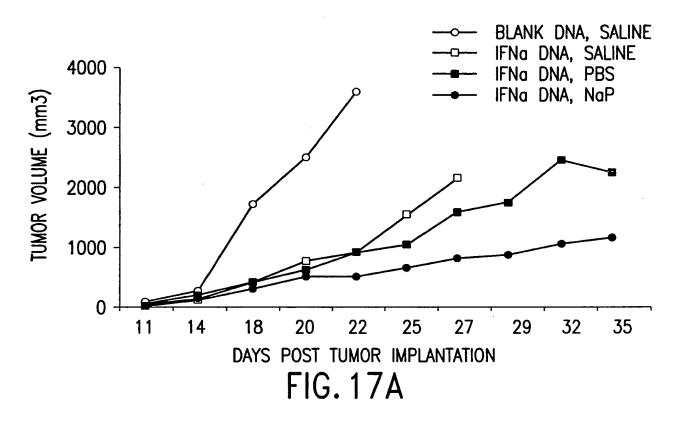
<u>nospomyu notyc</u>

Appl. No. 09/839,574; Group Art Unit: 1646 Dkt. No. 1530.0180002/EKS/EJH;

Inventors: Manthorpe et al.; Tel: 202/371-2600 Title: Compositions and Methods for in vivo Delivery o

Polynucleotide-Based Therapeutics

CLE EFFECTS ON IFNW pDNA MEDICATED ANTI-TUMOR EFFICACY



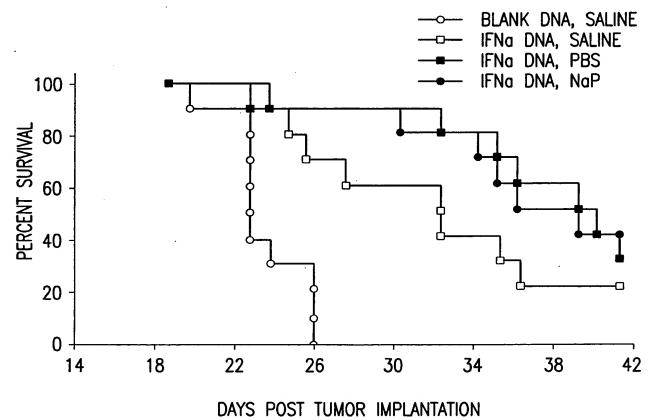
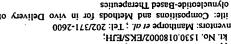
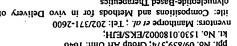
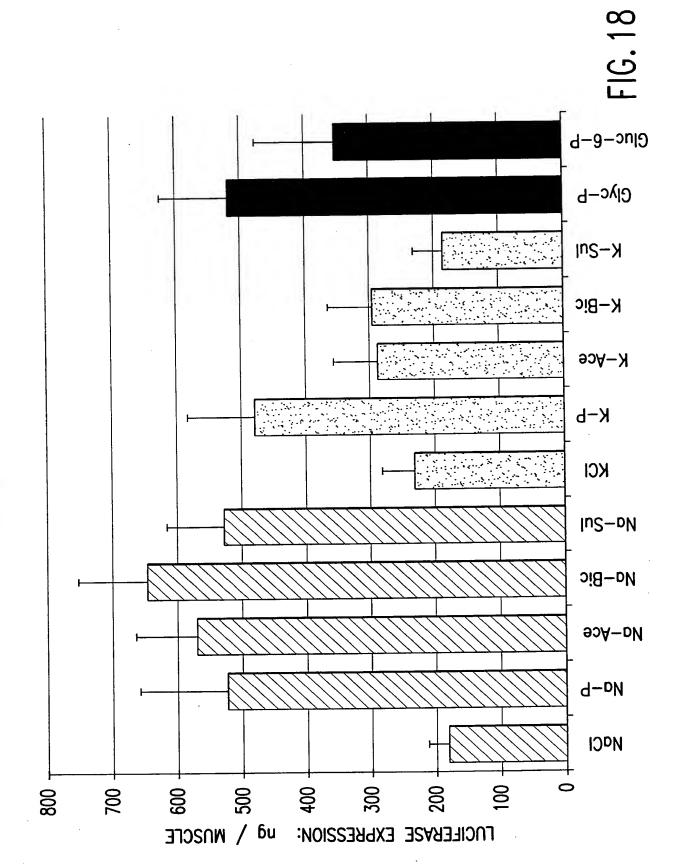


FIG. 17B

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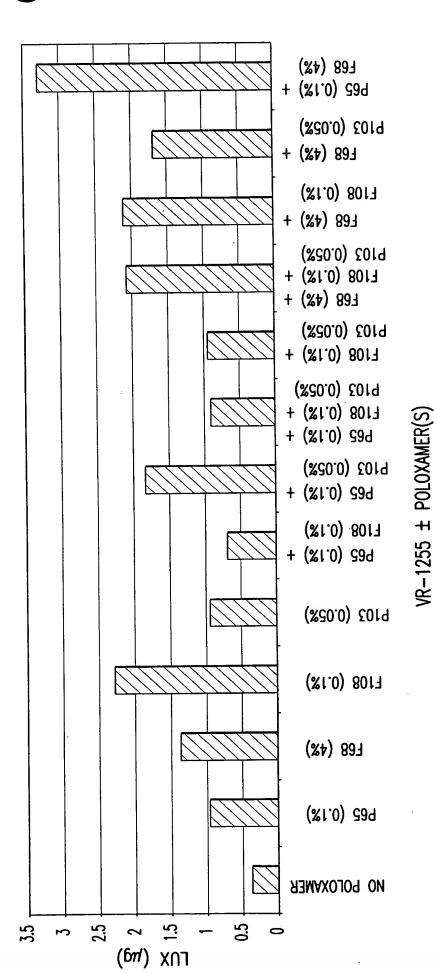


FIG. 19A

Title: Compositions and Methods for in vivo Delivery o Appl. No. 09/839,574; Group Art Unit: 1646 Dkt. No. 1530.0180002/EKS/EJH; Inventors: Manthorpe et al. ; Tel: 202/371-2600 Polynucleotide-Based Therapeutics

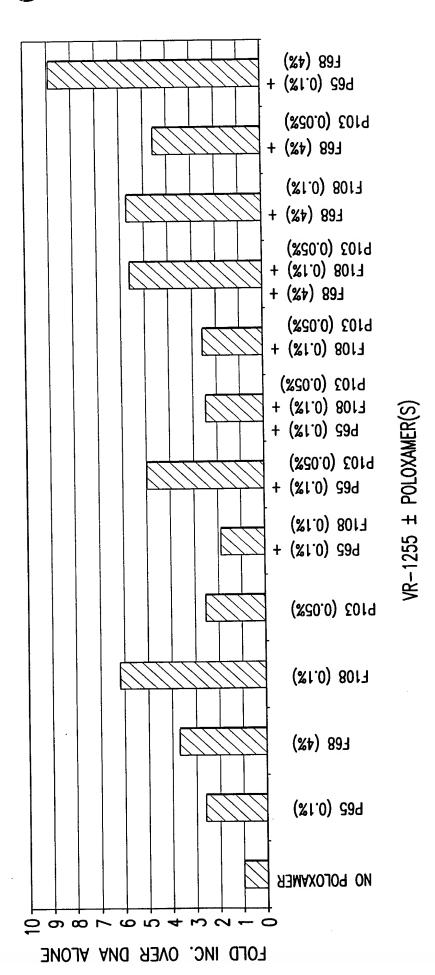
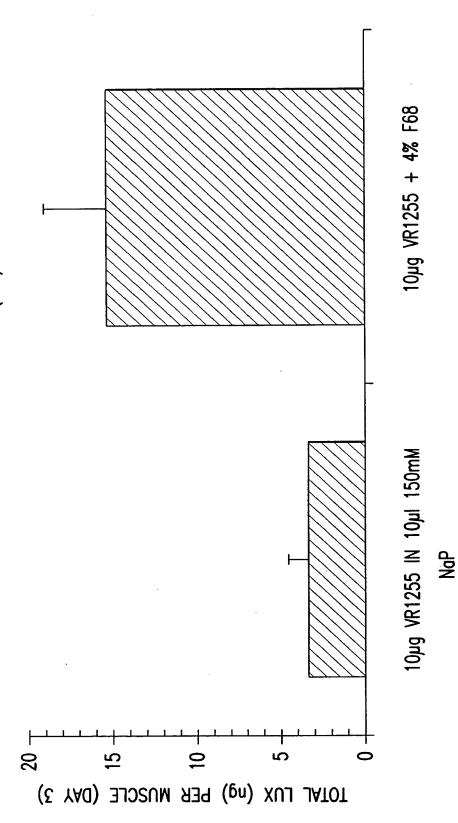


FIG. 19B

DAY 3 LUCIFERASE EXPRESSION AFTER INTRAMUSCULAR ADMINISTRATION OF VR1255 ± POLOXAMER (F68)



olynucleotide-Based Therapeutics

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nventors: Manthorpe et al.; Tel: 202/371-2600 ille: Compositions and Methods for in vivo Delivery of

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FIG. 20A

DAY 3 LUCIFERASE EXPRESSION AFTER INTRAMUSCULAR

ADMINISTRATION OF VR1255 ± POLOXAMER (25R2)

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Inventors: Manthorpe et al.; Tel: 202/371-2600
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Polynucleotide-Based Therapeutics

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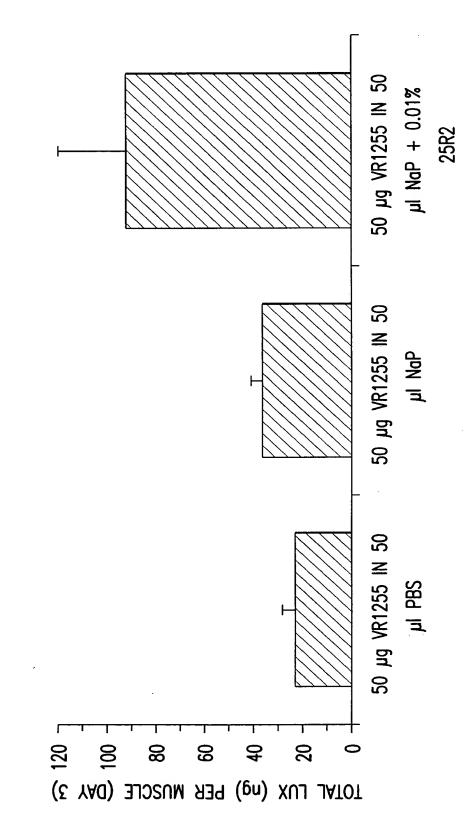


FIG. 20B

HEMATOCRIT LEVELS AFTER A SINGLE DOSE (1 µg) OF VR2901

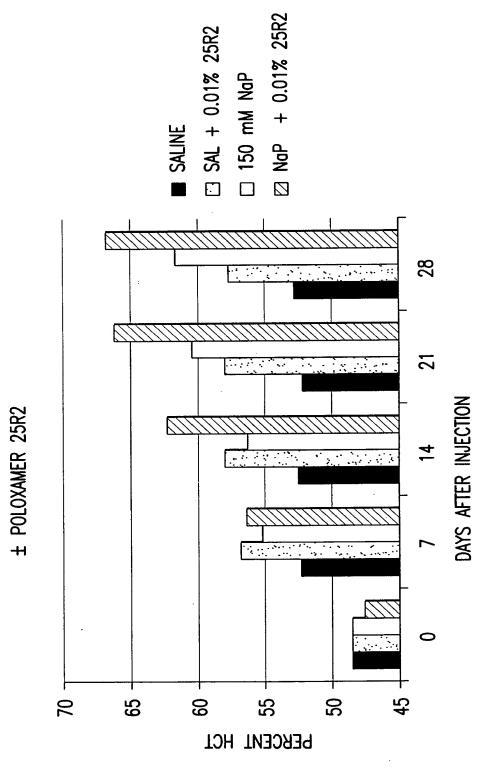


FIG. 21

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Dkt. No. 1530.0180002/EKS/EJH;
Inventors: Manthorpe et al.; 7el: 202/371-2600
Inventors: Manthorpe et al.; 7el: 202/371-2600
Polynucleotide-Based Therapeutics

ppl. No. 09/839,574; Group Art Unit: 1646 kt. No. 1530.0180002/EKS/EJH; nventors: Manthorpe et al.; Tel: 202/371-2600 itle: Compositions and Methods for in vivo Delivery of olynucleotide-Based Therapeutics

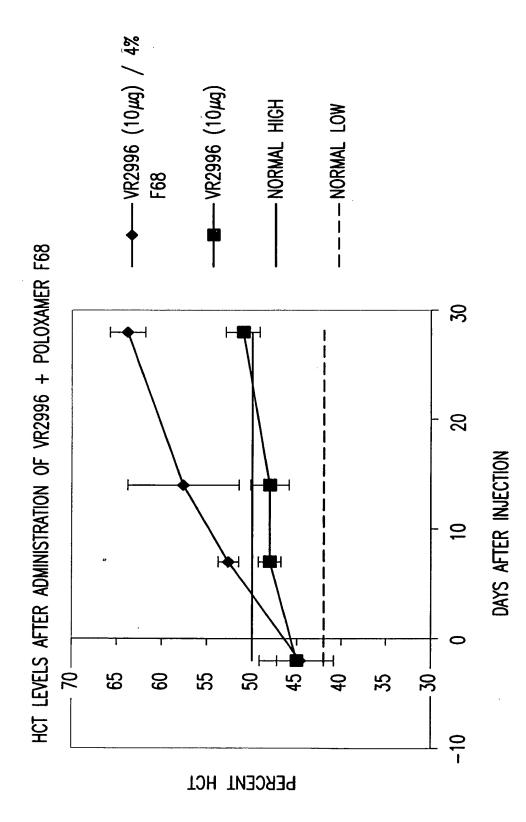
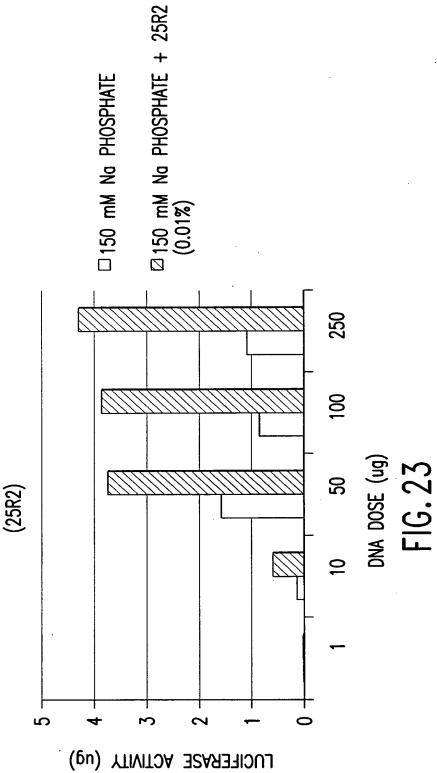
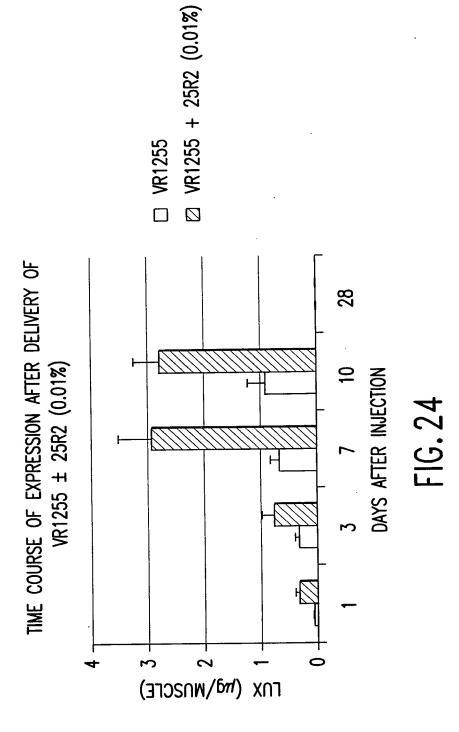


FIG. 22

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DKt. No. 1530.0180002/EKS/EJH;
Inventors: Manthorpe et al.; 7ei: 202/371-2600
Title: Compositions and Methods for in vivo Delivery o
Polynucleotide-Based Therapeutics

ppl. No. 09/839,574; Group Art Unit: 1646 kt. No. 1530.01 80002ZEKS/EJH; nventors: Manthorpe et al.; Tel: 202/371-2600 itle: Compositions and Methods for in vivo Delivery of olynucleotide-Based Therapeutics TRANSFECTION OF MOUSE RECTUS FEMORIS WITH VR1412 (pBgal) \pm POLOXAMER 25R2 (0.01%)

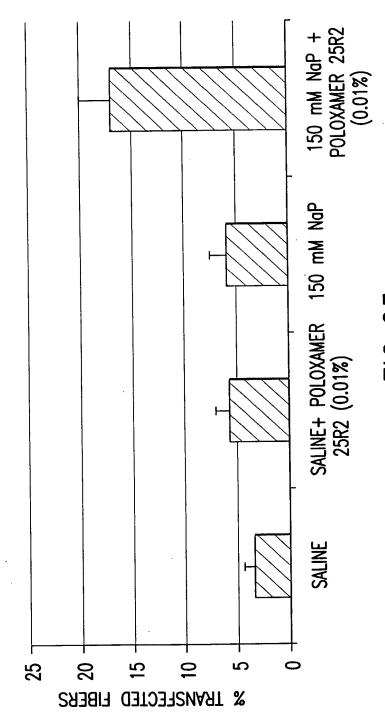
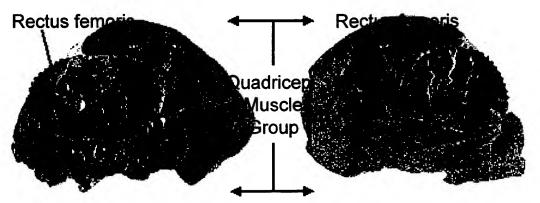


FIG. 25

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Targeted injections of 50 μg β-gal pDNA into murine rectus femoris (10 μm section stained with x-gal)



pDNA in saline, average transfection at 7 days

pDNA in Na-P + 25R2, average transfection at 7 days

FIG.26